REMARKS

The Examiner rejected claims 1-3, 5, 6, 8, 9, 13, 14, 16, and 18-20. Claims 1-3, 5, 6, 8, 9, 13, 14, 16, and 18-20 have been canceled without prejudice, and claims 21-40 have been added herein. Thus, claims 21-40 are pending. In addition, the specification has been amended to replace "Fig.2" with "Figure 2A and 2B" as suggested by the Examiner.

Applicants' specification fully supports new claims 21-40. For example, page 9, lines 7-19 of Applicants' specification discloses delaying polypeptide expression by a cell introduced into a mammal, to a time following the introduction of the cell into the mammal, while page 17, lines 6-8 discloses autologous cells transformed *in vitro*. Thus, no new matter has been added.

In light of the following remarks, Applicants respectfully request reconsideration and allowance of claims 21-40.

Claim objections

The Examiner objected to claims 1-3, 5, 6, 8, 9, 13, 14, 16, and 18-20 suggesting that the preamble of claims 1, 14, and 19 should read "encoding an immunogenic polypeptide." The Examiner also stated that the marked up copy of claim 18 is incorrect.

Claims 1-3, 5, 6, 8, 9, 13, 14, 16, and 18-20 have been cancelled herein. Thus, these objections are moot.

Rejections under 35 U.S.C. § 112, first paragraph

The Examiner rejected claims 1-3, 5, 6, 8, 9, 13, 14, 16, and 18 under 35 U.S.C. § 112, first paragraph, alleging that the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with the claims for the reasons of record.

Applicants respectfully disagree. Applicants' specification as filed fully enables claims 1-3, 5, 6, 8, 9, 13, 14, 16, and 18. To further prosecution, however, claims 1-3, 5, 6, 8, 9, 13, 14, 16, and 18 have been cancelled without prejudice. Thus, this rejection is moot.

New claims 21-28 recite methods for delaying enhanced expression of a polypeptide by a cell introduced into a mammal, to a time following the introduction of the cell into the mammal. The presently claimed methods require introducing a cell into a mammal exhibiting an immune

response against the recited polypeptide prior to the introducing step, where the cell (1) contains the recited vector and (2) is not maximally expressing the recited polypeptide during the introducing step. The presently claimed methods also require altering the concentration of the inducing agent to which the cell is exposed such that enhanced expression of the polypeptide by the introduced cell is induced at a time after the introducing step. Applicants' specification as filed fully enables the presently claimed methods. In fact, a person having ordinary skill in the art at the time Applicants filed would have been able, without undue experimentation, to (1) obtain cells having a vector containing a regulatable promoter operably linked to nucleic acid encoding a polypeptide, (2) introduce those obtained cells into a mammal, and (3) alter the concentration of an inducing agent to which the cells are exposed such that enhanced expression of the polypeptide is induced at a time after the introducing step. This is especially true given the many publications describing the use of regulatable promoters to regulate polypeptide expression. See, e.g., Applicants' specification at page 10, lines 9-12. Thus, Applicants' specification fully enables new claims 21-28.

New claims 29-34 recite isolated cells autologous to a human, while new claims 35-40 recite compositions containing a plurality of isolated cells autologous to a human together with a physiologically acceptable diluent. The claims require the cells to have a vector containing a regulatable promoter operably linked to a nucleic acid sequence encoding a polypeptide. The claims also require the human to exhibit an immune response against the polypeptide.

Applicants' specification as filed fully enables present claims 29-40. In fact, a person having ordinary skill in the art at the time Applicants filed would have been able, without undue experimentation, to obtain cells from a human and introduce the recited vector into those obtained cells. Thus, Applicants' specification fully enables new claims 29-40.

Rejections under 35 U.S.C. § 112, second paragraph

The Examiner rejected claims 1-3, 5, 6, 8, 9, 13, 14, 16, and 18-20 under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The Examiner stated that the claims are indefinite because several quoted phrases are unclear.

Applicants respectfully disagree. The meaning of claims 1-3, 5, 6, 8, 9, 13, 14, 16, and 18-20 is clear and definite. To further prosecution, however, claims 1-3, 5, 6, 8, 9, 13, 14, 16, and 18-20 have been canceled herein without prejudice. Thus, this rejection is moot.

Rejections under 35 U.S.C. § 102(b)

The Examiner rejected claims 1, 18, and 19 under 35 U.S.C. § 102(b) as being anticipated by Shockett *et al.* (*PNAS*, 92:6522-6526 (1995)) for the reasons of record. Applicants respectfully disagree. Claims 1, 18, and 19 are not anticipated by the Shockett *et al.* reference. Claims 1, 18, and 19, however, have been cancelled herein. Thus, this rejection is moot.

The Shockett *et al.* reference does not anticipate the new method claims 21-28. In fact, at no point does the Shockett *et al.* reference disclose introducing a cell into a mammal, where (1) the cell contains a vector having a regulatable promoter operably linked to nucleic acid encoding a polypeptide and (2) the mammal exhibits an immune response against the recited polypeptide prior to the introducing step. The Examiner acknowledged this in that the Examiner stated that "the prior art of record does not teach or suggest introducing a cell expressing a [an] immunogenic polypeptide as claimed into a mammal wherein the mammal has an immune response to the polypeptide prior to administering the cell." See, page 14 of the Office Action dated September 12, 2001.

The Examiner also rejected claims 14 and 16 under 35 U.S.C. § 102(b) as being anticipated by Hofmann *et al.* (*PNAS*, 93:5185-5190 (1996)) for the reasons of record. Applicants respectfully disagree. Claims 14 and 16 are not anticipated by the Hofmann *et al.* reference. Claims 14 and 16, however, have been cancelled herein. Thus, this rejection is moot.

New claims 29-34 recite isolated cells autologous to a human, while new claims 35-40 recite compositions containing a plurality of isolated cells autologous to a human together with a physiologically acceptable diluent. The claims require, *inter alia*, the human to exhibit an immune response against the recited polypeptide. At no point does the Hofmann *et al.* reference disclose such cells or compositions. Thus, the Hofmann *et al.* reference does not anticipate new claims 29-40.

Rejections under 35 U.S.C. § 103(a)

The Examiner also rejected claim 18 under 35 U.S.C. § 103(a) as being unpatentable over Hofmann *et al.* (*PNAS*, 93:5185-5190 (1996)) for the reasons of record. Applicants respectfully disagree. Claim 18 is not obvious in view of the Hofmann *et al.* reference. Claim 18, however, has been cancelled herein. Thus, this rejection is moot.

New claims 21-28 recite methods for delaying enhanced expression of a polypeptide by a cell introduced into a mammal, to a time following the introduction of the cell into the mammal. The presently claimed methods require introducing a cell into a mammal exhibiting an immune response against the recited polypeptide prior to the introducing step, where the cell (1) contains the recited vector and (2) is not maximally expressing the recited polypeptide during the introducing step. The presently claimed methods also require altering the concentration of the inducing agent to which the cell is exposed such that enhanced expression of the polypeptide by the introduced cell is induced at a time after the introducing step. At no point does the Hofmann *et al.* reference disclose such methods. Again, the Examiner acknowledged that "the prior art of record does not teach or suggest introducing a cell expressing a [an] immunogenic polypeptide as claimed into a mammal wherein the mammal has an immune response to the polypeptide prior to administering the cell." See, page 14 of the Office Action dated September 12, 2001. Thus, new claims 21-28 are patentable over the Hofmann *et al.* reference.

CONCLUSION

Applicants submit that claims 21-40 are in condition for allowance, which action is requested. The Examiner is invited to call the undersigned agent at the telephone number below if such will advance prosecution of this application. The Commissioner is authorized to charge any fees or credit any overpayments to Deposit Account No. 06-1050. Please change the

Attorney Docket No. to 07039-416001. Attached is a marked-up version of the changes being made by the current amendment.

Respectfully submitted,

Date: September 12, 2002

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Version with markings to show changes made

In the specification:

Paragraph beginning at page 7, line 12 has been amended as follows:

--Figures 2A and 2B show [Figure 2 shows] representative results confirming the regulation of the chTCR gene expression by tetracycline analogs. In Figure 2A, stable transfected uncloned JLAV12S (left hand side) and JN3S Jurkat (right hand side) cell populations were cultured for 48 hours in tetracycline-free medium (CM, upper row of panels) or in the presence of 1μg/ml of Tet (broken line) or Dox (solid line) (lower row of panels) and the surface expression of chTCRs was examined after staining with FITC-conjugated goat antisera to mouseλ light chain. Figure 2B shows a timecourse of inactivation of chTCR gene expression in JLAV12S cells zero hours (top left), 8 hours (top right), 12 hours (bottom left) or 24 hours (bottom right) after addition of Dox at 1 μg/ml. In both Figures 2A and 2B negative controls (FITC-conjugated goat antisera to mouse IgG) are overlaid (filled curve). The fluorescence channel number is plotted along the x axis, and the y axis represents the relative cell number.--

In the claims:

Claim 1-3, 5, 6, 8, 9, 13, 14, 16, and 18-20 have been cancelled without prejudice.